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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,960	02/04/2002	Ross Rabin	NEX83/D	5849

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,960	RABIN ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-44 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-44 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. There are (2) "Claim 25". The second misnumbered "claim 25" has be renumbered "claim 35" in accordance with 37 CFR 1.126.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 3 and 19, drawn to a nucleic acid ligand to HGF, wherein said ligand consists of SEQ ID NOs: 1-185, respectively, classifiable in class 536, subclass 24.5.

Group II. Claims 13, 15, and 35, drawn to a method for the treatment of a tumor, and a method for inhibiting angiogenesis, comprising administering a nucleic acid ligand to HGF, classifiable in class 514, subclass 44.

Group III. Claim 14, drawn to a method for determining the level of HGF in an individual, comprising providing a nucleic acid ligand to HGF, contacting a biological fluid from said individual with said nucleic acid ligand, and determining the amount of HGF that is bound to said nucleic acid ligand, classifiable in class 435, subclasses 6 and 91.2.

Group IV.	Claims 17, 18, 20-28, and 34, drawn to a nucleic acid ligand to c-met, classifiable in class 536, subclass 24.5.
Group V.	Claims 29-31, drawn to a method for the isolation of a nucleic acid ligand to c-met, classifiable in class 435, subclass 6.
Group VI.	Claims 32 and 33, drawn to a method for the treatment of a tumor and a method for inhibiting angiogenesis, comprising administering a nucleic acid ligand to c-met, classifiable in class 514, subclass 44.
Group VII.	Claims 36-38, drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, in combination with a nucleic acid ligand to VEGF and/or bFGF, classifiable in class 514, subclass 44.
Group VIII.	Claims 41 and 42, drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to at least two growth factor receptors, classifiable in class 514, subclass 44.
Group IX.	Claims 43 and 44, drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to at least two growth factor receptors, in combination with nucleic acids ligands to one or more growth factors, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons

The invention of Group I is related to the method inventions of Groups II and III as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product can be used in materially different processes of use. For example, nucleic acid ligands to HGF of Group I can be used as a hybridization probe to characterize HGF gene expression, which is a materially different process than a method for the treatment of a tumor, and a method for inhibiting angiogenesis as in Group II, and a method for determining the level of HGF in an individual as in Group III.

The inventions of Groups II and III are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Groups II and III are unrelated because Group II is drawn to a method for the treatment of a tumor, and a method for inhibiting angiogenesis, whereas Group III is drawn to a method for determining the level of HGF in an individual. For example, Group III requires determining the amount of HGF that is bound to a nucleic acid ligand to HGF, and thus recites an additional step that is not required of Group II. A search and examination of these methods in one patent application would result in an undue burden, since the searches for the methods are not co-extensive, the classification is different, and the two methods have different and noninterchangable steps, that lead to different ends. Furthermore, the methods of Groups II and

III are directed to different results and each set of Groups may be practiced without knowledge of or reference to the results of any other method. For these reasons, Groups II and III are separate and distinct from each other.

The invention of Group IV is related to the method inventions of Groups V and VI as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product can be used in materially different processes of use. For example, nucleic acid ligand to c-met of Group IV can be used as a hybridization probe to characterize c-met gene expression, which is a materially different process than a method for the isolation of a nucleic acid ligand to c-met as in Group V, and a method for the treatment of a tumor and a method for inhibiting angiogenesis, as in Group VI.

The inventions of Group II and Group VII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Group II and Group VII are unrelated because they employ different molecules with different chemical structures. The different inventions are drawn methods for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, **in combination with** nucleic acid ligands to growth factors of entirely different genes with very different physical properties and chemical structures (e.g. VEGF and/or bFGF). For example, Group II is drawn to a method for inhibiting tumor development, comprising administering only a nucleic acid ligand

to HGF. However, Group VII requires **combination therapy** using nucleic acid ligands to HGF, in addition to nucleic acid ligands to either VEGF and/or bFGF. Since nucleic acid ligands to VEGF and/or bFGF used in the claimed methods are structurally and functionally independent and distinct from nucleic acid ligands to HGF, it would constitute a serious burden on the Examiner to search nucleic acid ligands to physically and chemically different genes. Thus, they are patentably distinct from each other.

The inventions of Group II and Group VIII are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Groups II and VIII are unrelated because they employ different molecules with different chemical structures. The different inventions are drawn methods for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, and methods for inhibiting tumor development comprising administering nucleic acid ligands to at least two growth factor **receptors**. Since nucleic acid ligands to HGF, and nucleic acid ligands to growth factor **receptors** used in the claimed method are structurally and functionally independent and distinct, it would constitute a serious burden on the Examiner to search nucleic acid ligands to HGF and nucleic acid ligands to at least two growth factor **receptors**, since these are physically and chemically different genes. Thus, they are patentably distinct from each other.

The inventions of Group VIII and Group IX are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Groups VIII and IX are unrelated because they employ different molecules with

different chemical structures. The different inventions are drawn methods for inhibiting tumor development, comprising administering a nucleic acid ligand to at least two growth factor receptors, **in combination with** nucleic acid ligands to one or more growth factors. For example, Group VIII requires only nucleic acid ligands to at least two growth factor receptors. However, Group IX requires **combination therapy** using nucleic acid ligands to at least two growth factor receptors, in addition to nucleic acid ligands to one or more growth factors. Since nucleic acid ligands to at least two growth factor receptors used in the claimed method are structurally and functionally independent and distinct from nucleic acid ligands to one or more growth factors, it would constitute a serious burden on the Examiner to search nucleic acid ligands to two physically and chemically different genes. Thus, they are patentably distinct from each other.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate

in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the Examiner before the patent issues. See MPEP § 804.01.

Claims 1, 2, 4-12, and 16 are generic to the invention of Group I and will be examined limited to the elected invention.

If Group I is elected, a further restriction is required among the individual SEQ ID NOs. listed in claims 3 and 19 as follows:

Claims 3 and 19 are subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claims 3 and 19 specifically claim RNA ligands to HGF consisting of SEQ ID NOs: 1-185. Although the RNA ligands to HGF claimed each bind a HGF nucleic acid, the instant RNA ligands to HGF are considered to be unrelated, since each RNA ligands to HGF claimed is structurally and functionally independent and distinct for the following reasons: each RNA ligand to HGF has a unique nucleotide sequence, each RNA ligand to HGF binds a different and specific region of a HGF nucleic acid, and each RNA ligand to HGF has different binding affinities for HGF (per applicants' Figure 7B, Figure 8B, and Tables 2-5 in the specification). As such the Markush/genus of RNA ligands to HGF in claims 3 and 19 are not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the RNA ligands to HGF claimed in claims 3 and 19 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed RNA ligands to HGF. In view of the foregoing, one (1) RNA ligand to HGF is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) RNA ligand to HGF from claims 3 and 19. This is not a species election.

Claims 1, 2, 4-12, and 16 links inventions of Group I. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 11, 2, 4-12, and 16. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional

application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 39 and 40 are generic to the invention of Group VII and will be examined limited to the elected invention.

If Group VII is elected, Applicants a further restriction is required among the combination therapies listed in claims 36, 37, and 38 as follows:

A. drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, in combination with a nucleic acid ligand to VEGF, as recited in claim 36.

B. drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, in combination with a nucleic acid ligand to bFGF, as recited in claim 37.

C. drawn to a method for inhibiting tumor development, comprising administering a nucleic acid ligand to HGF, in combination with a nucleic acid ligand to VEGF, and a nucleic acid ligand to bFGF, as recited in claim 38.

The different inventions are drawn to methods utilizing nucleic acid ligands encoding entirely different genes with very different physical properties and chemical structures. For example, the nucleic acid ligand to VEGF is considered to be unrelated to the nucleic acid ligand to bFGF because each nucleic acid ligand is structurally different and has a unique sequence. If Applicants elect Group VII, Applicants are required to pick either A, B, or C, as listed above, since the inventions are drawn to methods utilizing nucleic acid ligands encoding entirely different genes with very different physical properties and chemical structures.

Claims 39 and 40 links inventions of Group VII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 39 and 40. Upon

the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
September 22, 2004

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